

What is claimed is:

1. A method for identifying one or more complexes from a library of complexes, wherein said complex or complexes are selected for their ability to perform a preselected or desired function on a target molecule or by having a pre-selected structure, each complex being designated a morphatide, said method comprising:

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(a) preparing a library of morphatides, comprised of:

(i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or more regions of randomized sequence;

(ii) one or more linker components; and

(iii) one or more agent molecules or type of agent molecules, linked to the scaffolding component by one or more type of linker components; and

(b) screening the library of morphatides prepared in step (a) by contacting, binding, or associating the morphatides with one or more suitable target molecules upon which a morphatide performs a preselected or desired function or to which a morphatide binds or associates through a pre-selected structure of said morphatide under conditions permitting said morphatide to perform said preselected or desired function on said target molecules or permitting said morphatide to bind or associate with said target molecules through the preselected structure;

(c) separating the morphatides performing the preselected or desired function or binding or associating through the preselected structure, from the library of morphatides and target molecules; thereby identifying one or more complexes from a library of complexes, wherein said complex or complexes are selected for

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their ability to perform a preselected or desired function on a target molecule or by having a pre-selected structure.

5 2. A method for identifying one or more complexes from a library of complexes, wherein said complex or complexes are selected for their ability to perform a preselected or desired function on a target molecule or by having a pre-selected structure, each complex being designated a
10 morphatide, said method comprising:

(a) preparing a library of morphatides, comprised of:
15 (i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or more regions of randomized sequence; and (ii) one or more agent molecules or type of agent molecules, associated, bound, or bonded to the scaffolding component;

20 (b) screening the library of morphatides prepared in step (a) by contacting, binding, or associating the morphatides with one or more suitable target molecules upon which a morphatide performs a preselected or desired function or to which a morphatide binds or associates through a pre-selected structure of said morphatide under conditions permitting said morphatide to perform said preselected or desired function on said target molecules or permitting said morphatide to bind or associate with said target molecules through
25 the preselected structure;

30 (c) separating the morphatides performing the preselected or desired function or binding or associating through the preselected structure, from the library of morphatides and target molecules; thereby identifying one or more complexes from a library of complexes, wherein said complex or complexes are selected for
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their ability to perform a preselected or desired function on a target molecule or by having a pre-selected structure.

5 3. The method of either of claims 1 or 2, wherein the separation of step (c) is performed by either (a) separating the morphatides which do not perform the preselected or desired function or which do not bind or associate through a pre-selected structure or (b)

10 separating the morphatides which perform the preselected or desired function or which bind or associate through a pre-selected structure.

15 4. The method of either of claims 1 or 2, wherein said target molecule is bound to a solid support.

20 5. The method of either of claims 1 or 2, wherein the preselected or desired function performed by the complex(es) on a target molecule is selected from the group consisting of binding to or associating with said target molecule; reacting with said target molecule and changing the property of said target molecule; having an affinity for and binding to a specific ligand; performance of a biological activity, wherein said biological activity is selected from the group consisting of antimicrobial activity, antitumor activity, enzyme inhibiting activity, enzyme enhancing activity, receptor binding activity, growth promotion activity, antibody binding activity; formation of a biofilm; enzymatic activity, immune modulating activity, cell signaling activity, polymerizing activity, and encapsulating activity.

25 30 35 6. The method of either of claims 1 or 2, wherein said contacting, binding or association is selected from the group consisting of multiple complexes acting on a single target molecule, a single complex acting on multiple target

molecules, components of one or more complexes acting on multiple target molecules, components of one or more complexes acting on a single target molecule, and multiple complexes acting on multiple target molecules.

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7. The method of either of claims 1 or 2, wherein said scaffolding component comprises naturally occurring nucleotides, novel or unique bases, base analogs; synthetically generated nucleic acids, nucleic acid like molecules, and nucleic acid analogs; or any combination thereof.

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8. The method of claim 7, wherein the nucleic acid like molecule is a difluorotoluene or related deoxynucleoside.

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9. The method of either of claims 1 or 2, wherein said scaffolding component consists of subunits which are capable of being incorporated by one or more nucleic acid polymerases or reverse transcriptases and which can, when polymerized, generate hybridizable polymers with hydrogen bonding or hybridizable polymers without hydrogen bonding.

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10. The method of either of claims 1 or 2, wherein said scaffolding component comprises nucleic acids having regions of conserved sequences and one or more regions of randomized sequences.

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11. The method of either of claims 1 or 2, wherein the scaffolding component(s) are comprised of two fixed regions of nucleotides and one region of randomized nucleotides between the two fixed regions.

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12. The method of claim 1, wherein the linker component is associated to a base of the scaffolding component either before or after the scaffolding component is made.

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13. The method of either of claims 10 or 11, wherein the randomized region is comprised of:

(a) three of the four bases occurring with similar frequency; and

(b) one of the four bases occurring at a rare frequency.

5 14. The method of claim 13, wherein one of the bases occurring with similar frequency is associated with or binds with the linker component.

10 15. The method of claim 13, wherein one of the four bases occurring at a rare frequency is associated with or binds with the linker component.

15 16. The method of claim 14, wherein the position of the base with the linker attached is determined by nucleotide sequencing or mass spectrophotometry.

20 17. The method of claim 7, wherein each scaffolding component comprises more than one different nucleic acid base being attached to a linker component, said nucleic acid base being incorporated into the scaffolding component either during PCR amplification or during synthesis of the nucleic acids.

25 18. The method of claim 17, wherein the incorporated nucleic acid base to which the linker component is attached is a rare base.

30 19. The method of claim 17, wherein the base to which the linker is attached is modified, said modification being by chemical reaction either before or after incorporation during PCR amplification or during synthesis of the nucleic acids.

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20. The method of claim 17, wherein the incorporated nucleic acid base to which the linker component is attached is a different modified base, said base being any of the four bases or analogs of said bases, said base being modified by
5 a reaction.

21. The method of claim 17, wherein the incorporated base to which the linker component is attached is located internally in the scaffolding component.

10 22. The method of claim 1, wherein one or more of said linker components are either reversible or non-reversible, and wherein one or more of said linker components comprise reversibly connectable components or parts.

15 23. The method of claim 1, wherein one or more of said linker components cannot be amplified in vitro or in vivo.

20 24. The method of either of claims 1 or 2, wherein one or more of said scaffolding components associated with one or more of said linker components is amplifiable in vitro or in vivo.

25 25. The method of claim 1, wherein said one or more of said linker components connected to one or more of said agent molecules cannot be amplified in vitro or in vivo.

30 26. The method of claim 1 or 2, wherein the entire morphatide is amplifiable.

27. The method of claim 30, wherein a first linker component either reversibly or non-reversibly associated with a scaffolding component and a second linker component either reversibly or non-reversibly associated with an agent molecule are connected together to generate a scaffolding

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component linked to an agent molecule by the connectable first and second components of said linker component.

28. The method of claim 1, wherein the linker component is
5 selected from the group consisting of a phenyl-boronic acid linker, a thio linker, and a biotin-streptavidin linker.

29. The method of claim 28, wherein the thio linker is cysteine.
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30. The method of claim 2, wherein the scaffolding component is associated to one or more agent molecules, wherein said agent molecule is a peptide by a peptide bond.
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31. The method of claim 1, wherein the linker component is selected from the group consisting of a nucleic acid binding protein and a chelating molecule.
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32. The method of claim 1, wherein the linker component is either bound covalently to either the scaffolding component or to the agent molecule or the linker component is bound noncovalently to either the scaffolding component or to the agent molecule.
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33. The method of either of claims 1 or 2, wherein said agent molecules are selected from the group consisting of naturally occurring polymers, synthetically generated polymers, and non-polymeric molecules.
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34. The method of either of claims 1 or 2, wherein the library of complexes is prepared by:
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(a) coupling the linker molecules or components of the linker molecules to either the scaffolding components, to form scaffolding component-linker molecules or to the agent

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molecules, to form agent molecule-linker molecules; and
(b) generating a linkage between the scaffolding component-linker molecules and the agent molecules or between the scaffolding components and the agent molecule-linker molecules to yield the complexes, thereby preparing a library of complexes.

35. The method of claim 34, wherein said scaffolding components
10 are prepared for coupling to linker molecules via chemical reaction yielding modified nucleotides.

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36. The method of claim 21, wherein said chemical reaction involves treating the scaffolding components with one or more mutagens to add one or more base specific or non-specific adduct(s), resulting either in adducted scaffolding molecules, that enable increased reactivity of the base to the linker or directly to the agent molecules or in adducted scaffolding molecules, said adduct acting as either a linker or an agent molecule.

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37. The method of either of claim 36, wherein the adducted scaffolding components are amplifiable.

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38. The method of either of claim 36, wherein said mutagen is UV light, any other nucleic acid mutagen, or a nucleic acid binding protein.

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39. The method of claim 21, wherein said chemical reaction involves treating scaffolding components with Maxam & Gilbert based chemistries to generate increased reactivity of one or more bases to a linker or to an agent molecules.

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40. The method of claim 34, wherein said scaffolding components are prepared for coupling to the linker molecules via a non-chemical reaction yielding modified nucleotides.

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41. The method of claim 40, wherein said non-chemical reaction
is an enzymatic reaction.

42. The method of either of claims 1 or 2, said method further
comprising after step (b):
(a) disassociating the scaffolding component of the complex
performing the preselected or desired function from the
agent molecule or molecules;
(b) generating modified scaffolding components;
(c) associating the different scaffolding molecules with
agent molecules to generate different morphatides;
(d) rescreening the different morphatides by repeating
steps (b) and (c) of claims 1 or 2 to identify new desired
candidate morphatides.

43. The method of claim 42, wherein said modification of
scaffolding components occurs via a random or directed
mutagenesis technique.

44. The method of claim 43, wherein said random or directed
mutagenesis techniques are selected from the group
consisting of error-prone PCR or sexual PCR by performing
a suitable number of cycles on the scaffolding components,
resulting in one or more base changes in some percentage of
the scaffolding components; cassette mutagenesis; and site
directed mutagenesis.

45. The method of claim 42, wherein one or more of said agent
molecules in step (c) are different from the agent
molecules utilized in the morphatides of the prior round of
screening for identification of morphatides performing the
preselected or desired function.

46. The method of either of claims 1 or 2, for identifying a
different morphatide further comprising:
(a) separating the scaffolding components from the agent

molecules;

(b) performing a suitable number of cycles of error prone PCR on the scaffolding components, resulting in one or more base changes in some percentage of the scaffolding component;

(c) reconnecting the scaffold component to the agent component; and

(d) repeating steps (a) through (d) of claims 1 or 2, thereby identifying a different morphatide.

10 47. The method of claim 42, wherein the morphatide comprises a linker component, wherein in step (a) one part of a linker remains attached to the scaffold component and another part of the linker remains attached to the agent molecule and wherein in step (c) both parts of the linker are connected, thereby reconnecting the scaffold component to the agent component or wherein the connection between the agent molecule and the scaffolding component is by a plurality of the linker components.

15 48. The method of claim 42, wherein the scaffolding components are characterized by cloning and nucleotide sequencing before reattachment of the agent molecule in step (c).

20 25 49. The method of either of claims 1 or 2, further comprising:

(a) creating a mimic of the identified morphatide; and

(b) using the mimic for a desired application.

30 50. The method of either of claims 1 or 2, further comprising:

(a) separating scaffolding components with attached linker components or parts of the linker components from the agent molecules of the previously identified Morphatides;

(b) combining the scaffolding components with attached linker components or parts thereof with scaffolding components comprising a same nucleic acid sequence as the scaffolding components, said nucleic acid sequence not

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being attached to or associated with a linker components or parts thereof, thereby resulting in nucleic acid sequences without the one or more linker sites;

(c) using sexual PCR to fragment and reassemble the nucleic acid sequences, resulting in elimination of linker component sites which do not contribute to the binding of the morphatide, thereby generating new scaffolding components similar but not identical to the scaffolding components of step (a);

10 (d) reattaching or association agent molecules to the new scaffolding components of step (c), thereby generating another set of Morphatides.

51. A method of identifying a presence of a substance in a sample from a subject, comprising:

(a) obtaining a sample;

(b) contacting the sample with one or more types of morphatide identified by the method of either of claims 1 or 2 so as to form a complex between the morphatide and the

substance present in the sample.

thereby identifying the presence of the substance in the sample from the subject.

25 52. The method of claim 51, wherein step (c) is performed by PCR amplification, ethidium bromide staining or labeling selected from the group consisting of radioactive isotope, enzyme, dye, biotin, a fluorescent label, a chemiluminescent label and a ligand.

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53. The method of claim 51, wherein the detection of the complex formed in step (c) comprises identification of an occurrence selected from the group consisting of binding to or associating with a target molecule; having an affinity for and binding to a specific ligand; performance of a

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biological activity, wherein said biological activity is selected from the group consisting of antimicrobial activity, antitumor activity, enzyme inhibiting activity, enzyme enhancing activity, receptor binding activity, growth promotion activity, antibody binding activity; formation of a biofilm; enzymatic activity, immune modulating activity, cell signaling activity, polymerizing activity, and encapsulating activity.

10 54. A method of diagnosing a subject wherein detection of a complex in step (c) of claim 51 is indicative of a disease.

15 55. The method of claim 51, wherein the sample is a body fluid or a tissue specimen.

20 56. The method of claim 55, wherein the body fluid is selected from the group consisting of blood, serum, plasma, urine, saliva, nasal mucosal discharge, vaginal mucosal discharge, anal mucosal discharge, peritoneal fluid, cerebro-spinal fluid, and lymphatic fluid.

25 57. The method of claim 51, wherein the substance whose presence is identified is selected from the group consisting of hormones, enzymes, proteins, cancer/tumor cells, pathogens, and drugs.

58. The method of claim 51, wherein the subject is bacterial cells, a plant, a microbe, an insect, a fish, or a mammal.

30 59. The method of claim 58, wherein the mammal is a human.

60. A morphatide capable of effectively binding to, crosslinking with, or reacting with multiple types of molecules.

35 61. A morphatide capable of effectively binding to, crosslinking

with, or reacting with one type of molecule.

62. The morphatide of either of claims 60 or 61, wherein binding to, crosslinking with, or reacting with the molecules is selected from the group consisting of binding to or associating with a target molecule; having an affinity for and binding to a specific ligand; performance of a biological activity, wherein said biological activity is selected from the group consisting of antimicrobial activity, antitumor activity, enzyme inhibiting activity, enzyme enhancing activity, receptor binding activity, growth promotion activity, antibody binding activity; formation of a biofilm; enzymatic activity, immune modulating activity, cell signaling activity, polymerizing activity, and encapsulating activity.

63. A composition comprising a morphatide effective to treat a subject and a pharmaceutically acceptable carrier.

64. The method of administering the composition of claim 63, wherein the administration is intravenous, intraperitoneal, intrathecal, intralymphatical, intramuscular, intralesional, parenteral, epidural, subcutaneous; by infusion, liposome-mediated delivery, aerosol delivery; topical, oral, nasal, anal, ocular or otic delivery.

65. The morphatide of either of claims 60 or 61, conjugated to a therapeutic agent.

66. The morphatide of claim 65, wherein the therapeutic agent is a radioisotope, toxin, toxoid, or chemotherapeutic agent.

67. A composition comprising the conjugated morphatide of claim 65 and a pharmaceutically acceptable carrier, wherein the morphatide is selected from either a morphatide which is

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capable of being degraded or a morphatide which is incapable of being degraded after administration to a subject.

5 68. A morphatide labeled with a detectable marker.

69. The morphatide of claim 68, wherein the detectable marker is selected from the group consisting of a radioactive isotope, enzyme, dye, biotin, a fluorescent label, a chemiluminescent label and a ligand.

10 70. The composition of claim 67, wherein the morphatide is incapable of being degraded further comprising a stabilizer molecule for increasing the half-life of the morphatide in the blood stream.

15 71. The composition of claim 70, wherein the stabilizer is polyethyleneglycol.

20 72. A method of treating a subject with the composition of either of claims 63 and 67.

25 73. A method of drug delivery to a target in the body of a subject comprising administration to a subject of the composition of either of claims 63 and 67, thereby delivering the drug to the target.

30 74. The method of claim 67, wherein the degradation is performed by either of a nuclease or protease.

35 75. A method of drug delivery to a target in the body of a subject comprising administration to a subject of the composition of claim 63, wherein the morphatide is incapable of being degraded or is slowly degraded after administration to the subject, thereby delivering the morphatide-bound drug to the target.

76. The method of claim 75, wherein the morphatide-bound drug is administered, wherein the administration is intravenous, intraperitoneal, intrathecal, intralymphatical, intramuscular, intralesional, parenteral, epidural, subcutaneous; by infusion, liposome-mediated delivery, aerosol delivery; topical, oral, nasal, anal, ocular or otic delivery.

10 77. The method of claim 1, wherein the morphatide is capable of binding to any component of an antibody molecule, said antibody having a constant and variable region.

78. A morphatide identified according to the method of claim 1.

15 79. A morphatide identified according to the method of claim 42.

80. A morphatide identified according to the method of claim 46.

20 81. A morphatide identified according to the method of claim 50.

82. A method of increasing the binding affinity of a morphatide for a selected target molecule, said morphatide comprising a nucleic acid scaffold and one or more agent molecules;

25 said method comprising:

(a) amplifying the nucleic acid scaffold of the morphatide;

(b) generating modified scaffolding components;

(c) associating the different scaffolding components with said agent molecules to generate different morphatides;

(d) screening the morphatides for ability to bind to the selected target; and

(e) separating morphatides with an increased binding affinity for said target.

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83. A method of increasing the binding affinity of a morphatide for a selected target molecule, said morphatide comprising a nucleic acid scaffold and one or more agent molecules; said method comprising:
5 (a) performing a suitable number of cycles of error prone PCR on the scaffolding component of the morphatide, resulting in one or more base changes in some percentage of the scaffolding component;
10 (b) associating the different scaffolding components with said agent molecules to generate different morphatides;
(c) screening the morphatides for ability to bind to the selected target; and
15 (d) separating morphatides with an increased binding affinity for said target.

84. A method of increasing the binding affinity of a morphatide for a selected target molecule, said morphatide comprising a nucleic acid scaffold, a linker component and one or more agent molecules; said method comprising:
20 (a) amplifying the scaffold component of the morphatide;
(b) associating said scaffold components with linker components or parts thereof;
(c) combining the scaffolding components with attached
25 linker components or parts thereof with scaffolding components comprising the same nucleic acid sequence as the scaffolding components, said nucleic acid sequence not being attached to or associated with a linker components or parts thereof, thereby resulting in nucleic acid sequences
30 without the linker sites;
(d) using sexual PCR to fragment and reassemble the nucleic acid sequences, resulting in elimination of linker component sites which do not contribute to the binding of the morphatide, thereby generating new scaffolding components similar but not identical to the scaffolding
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components of step (a);
(e) associating agent molecules to the new scaffolding components of step (d), thereby generating a different set of morphatides;
5 (f) screening the morphatides for ability to bind to the selected target; and
(g) separating morphatides with an increased binding affinity for said target.

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